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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,121	05/23/2006	David B. Smithrud	91830.0538278	2766

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EXAMINER	
STONE, CHRISTOPHER R	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
08/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@fbtlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,121	SMITHRUD, DAVID B.	
	Examiner	Art Unit	
	CHRISTOPHER R. STONE	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 28-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 5, 2009, has been entered.

Applicants' arguments, filed June 5, 2009, have been fully considered but are moot in view of new grounds of rejection. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1-35 are pending. Claims 1-18 and 28-35 are withdrawn as being drawn to nonelected species. Claims 19-27 are currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-27 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as host-rotaxanes comprising a polymer (e.g. substituted methylene chains with repeating CH_2 subunits, Figs. 1 and 2), which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 19-27 are directed to host-rotaxanes which do not comprise a polymer, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of host-rotaxanes which do not comprise a polymer meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed host-rotaxanes which do not comprise a polymer, regardless of the complexity or simplicity of the method of isolation. For example, it is unclear what linear molecules, other than

polymers, would be used to make the linear segment of the host-rotaxane. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> Therefore, only the above chemically structurally defined chemicals, but not the

full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-27 are drawn to a host-rotaxane, wherein the host-rotaxane is not a polymer. It is unclear what linear molecules, other than polymers, would be used to make the linear segment of the host-rotaxane, thus it is unclear what host-rotaxanes the claim intends to encompass.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-21 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yui et al (US 2003/0171573 A1) in view of Suzuki et al (US 6,242,430 B1).

Yui et al teaches a method of delivering an agent (e.g. a drug) to a subject, comprising administering to the subject a composition comprising a host-rotaxane and a bound guest molecule (e.g. the drug guest molecule concurrently administered with the host rotaxane), wherein the guest molecule comprises an active agent (a drug); wherein the host-rotaxane comprises (a) at least one linear component having a first and second terminal end; (b) at least one cyclic component; and (c) at least one blocking group (e.g. bulky substituents which cap the ends of the linear molecule to prevent the linear molecule from detreading from the cyclic component); wherein the at least one linear component is disposed in the cyclic component and the at least one blocking group is present at the first, second or both terminal ends of the linear component; and wherein at least one of the blocking groups on the first or second terminal end of the linear molecule of the host-rotaxane comprises a guest binding element for associating with the guest molecule to form a host-guest complex (paragraph 0085, 0088 and claim 16). The host-rotaxane is taught to further comprise a target-binding moiety/recognition element (a ligand, e.g. a growth factor or cytokine) linked to the host-rotaxane via an ester linkage, cleavable by endogenous esterases (paragraphs 0057-0060 and Table 1), wherein the recognition element is present in a convergent arrangement with the guest binding (bulky substituent/blocking group) element (biotin, figure 3). Yui et al further teaches that the linear element of the host rotaxane can be made from any linear molecule (paragraph 0064); however Yui et al does not explicitly teach that the linear element of the host-rotaxane is not a polymer.

Suzuki et al (US 6,242,430 B1) teaches a method comprising concurrently administering a host-rotaxane and an agent (a flourophore), wherein the host-rotaxane is a methylene chain, i.e. the host-rotaxane is not a polymer, in a pharmaceutically acceptable carrier, water, a liquid filler or diluent (Figures 2 and 3, column 1, lines 47-65 and column 10, lines 33-40). Suzuki et al further teaches the rotaxane complex is useful for medical diagnosis and treatment (column 10, lines 33-40 and column 11, lines 3-6). Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to us a methylene chain as the linear component in the rotaxane of Yui et al, since Yui et al teaches that any linear molecule is appropriate to serve as said component and Suzuki et al teaches that methylene chains (i.e. non-polymeric molecules) are appropriate to serve as the linear component in rotaxane complexes for therapeutic purposes, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Claims 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yui et al (US 2003/0171573 A1) and Suzuki et al (US 6,242,430 B1), as applied above, further in view of Guillemard et al (Cancer Research, Vol. 61, p. 694-699, 2001).

Yui et al (US 2003/0171573 A1) and Suzuki et al (US 6,242,430 B1) teach the aforementioned method but do not explicitly teach the that the active agent (drug)/host-rotaxane conjugate effectively targets the agent (drug) into the cytoplasm of the cells of cancer, tumors, etc. at a higher rate relative to the unconjugated agent. Guillemard et al teaches that paclitaxel (a cancer drug) conjugated to a growth factor receptor ligand effectively targets the drug into the cytoplasm of the cells of cancer, tumors, etc. at a

higher rate relative to the unconjugated agent (abstract, p. 694, right column, paragraphs 2-4, p. 695, left column, last full paragraph, p. 697, 697, right column, paragraphs, first full paragraph and p. 698, Improved Efficacy heading). Therefore it would have been prima facie obvious to one of ordinary skill in the art to prepare the conjugate of Yui et al and Suzuki et al such that that the active agent (drug)/host-rotaxane conjugate effectively targets the agent (drug) into the cytoplasm of the cells of cancer, tumors, etc. at a higher rate relative to the unconjugated agent, since Yui et al teaches that growth factor receptor ligands can act to target the host-rotaxane drug complex and Guillemard et al teaches that targeting cancer drugs to cancer cells using such ligands can increases the cellular uptake of the drug relative to unconjugated forms, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yui et al (US 2003/0171573 A1) and Suzuki et al (US 6,242,430 B1), as applied above, further in view of Goodman and Gilman's, The Pharmacological Basis of Therapeutics.

Yui et al (US 2003/0171573 A1) and Suzuki et al (US 6,242,430 B1) teach the aforementioned method but do not explicitly teach the routes of administration of claim 23.

Goodman's and Gilman's teaches that it is common practice in the pharmaceutical art to select an appropriate route of administration (parenteral, oral, etc.) and carrier system (solid, aqueous solution, oily solution, etc.) to optimize bioavailability for a particular drug (Goodman and Gilman's, p. 5, right column through p. 6 left

column, Table 1-1). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to administer the composition via any conventional route of administration in conjunction with a conventional carrier system appropriate for said route (e.g. parenterally with a diluent or orally with an encapsulating material), since it is common practice in the pharmaceutical art to select an appropriate route of administration (parenteral, oral, etc.) and carrier system (solid, aqueous solution, oily solution, etc.) to optimize bioavailability for a particular drug (Goodman and Gilman's, p. 5, right column through p. 6 left column, Table 1-1). Thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10August2009
CRS

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645